Remarks

Rejection of Claims 1, 2, and 5-13 under 35 U.S.C. §102(a)

Claims 1, 2, and 5-13 stand rejected as anticipated by Lal et al. (J. Natl. Cancer Insti., 93: 1337-1343, 2001). This rejection is respectfully traversed.

Claims 1, the only independent claim of the rejected set, is directed to a method in which an expression product of the gene signal sequence receptor, delta (translocon-associated protein delta; hereinafter SSR4), is detected in a first brain tissue sample suspected of being neoplastic and compared to expression of the gene in a second brain tissue sample which is normal.

The rejection characterizes Lal et al. as using the same gene and gene product to identify a human glioma. Office Action at page 3, lines 10-11. Moreover, the rejection characterizes Lal et al. as having "compared cancerous tissue to normal tissue (p. 1338, column 1)." Office Action at page 3, lines 18-19. However, the rejection mischaracterizes the teachings of Lal et al.

Lal et al., compares gene expression of a glioblastoma cell line under two types of conditions: hypoxic and normal oxygen levels. "[W]e studied the global expression pattern of malignant cells by varying only oxygen concentration. A human glioblastoma multiforme (GBM) cell line was our hypoxia response model…" Lal et al., page 1337, paragraph spanning column 2 and column 3. "Cell lines were grown with the use of standard cell culture techniques either in equilibrium with atmospheric oxygen or in an Environmental Chamber (Sheldon Manufacturing, Cornelius, OR) with 1.5% oxygen, which approximates the tumor hypoxia levels (12) for hypoxic conditions." Lal et al., page 1337, column 3, lines 22-27. "Messenger RNA (mRNA) was isolated from normal and hypoxic cells, and SAGE libraries were constructed as described previously *(11)*." Page 1338, column 1, lines 6-8. "For western blot analysis, total cell lysates were prepared from cells grown either at normal oxygen or at 1.5% oxygen for the indicated times." Lal et al., page 1338, column 1, last paragraph. "[W]e cultured human glioblastoma cells either in 1.5% oxygen for 24 hours or in normal atmospheric oxygen….Two SAGE libraries were constructed from hypoxic D247-MG cells and the normal oxygen control." Lal et al., page 1338, column 3, second full paragraph.

Thus, when Lal et al., provides results in Table 1, entitled "Genes induced by hypoxia in glioblastoma cell line D247-MG, and provides data regarding fold-increases in SAGE and PCR, the fold-increases refer to a comparison of hypoxic to normal oxygen conditions for the single

glioblastoma cell line D247-MG. As stated in the last footnote to Table 1: "Fold increases are the ratio of hypoxic to normal transcript levels for SAGE and real-time PCR."

Contrary to the U.S. Patent and Trademark Office's characterization of the data in Lal et al., they do not represent a comparison of glioblastoma to normal cells. Thus Lal et al., does not anticipate the method of independent claim 1 or any of its dependent claims.

Withdrawal of this rejection is respectfully requested.

Rejection of Claims 3 and 4 Under 35 U.S.C. §112, first paragraph

Claims 3 and 4 are rejected as not enabled in the specification. This rejection is respectfully traversed.

Claims 3 and 4 recite increased expression in suspect brain sample relative to a normal brain sample of at least 5-fold or at least 10-fold. The U.S. Patent and Trademark Office urges that these claims are not enabled because applicants teach using a threshold of 2-fold and because Lal et al., teach an increase of 2.3-fold in Table 1. As discussed above, Lal et al., teach an increase of hypoxic over non-hypoxic glioblastoma cells. Lal et al., does not teach any comparison or any level of glioblastoma to normal tissue. Thus the Lal et al. teaching is irrelevant. The U.S. Patent and Trademark Office has no basis to challenge the teachings of claims 3 and 4, as is required to make a *prima facie* case of non-enablement. Absent any factual basis, this rejection should be withdrawn.

Allowance of all pending claims is respectfully requested.

Respectfully submitted,

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